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Determination, occurrence, and treatment of saccharin in water: A review

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Abbreviations: AC: activated carbon; ACE: acesulfame; AOPs: advanced oxidation processes; ASP: aspartame; ASs: artificial sweeteners; BC: biochar; BL: black light; C4D: capacitively coupled contactless conductivity detection; CE: electrophoresis; COD: chemical oxygen demand; CYC: cyclamate; d-SPE: dispersive solid-phase extraction; DI: direct-injection; DWTPs: drinking water treatment plants; EDCs: endocrine disrupting chemicals; ESI: electrospray ionization; FIA: flow injection analysis; GAC: granular activated carbon; GC: gas chromatography; HPLC: high-performance liquid chromatography; HR: high resolution; IC: ion chromatography; ID: isotope-dilution; ILOQs: instrumental limits of quantifications; LED: light-emitting diode; LODs: limits of detection; LOQs: limits of quantitation; MDCs: derived porous carbons; MOF: metal-organic framework; MS/MS: tandem mass spectrometry; OMW: olive mill wastewater; PAC: powdered activated carbon; PDS: sodium peroxydisulfate; PLE: pressurised liquid extraction; PMS: peroxomonosulfate; POPs: persistent organic pollutants; Q: quadrupole; RO: reverse osmosis; RP-HPLC: reversed-phase high-performance liquid chromatography; SAC: saccharin; SBRs: sequencing batch reactors; SPE: solid phase extraction; SUC: sucralose; TLC: thin-layer chromatography; TOF: time-of-flight; TQ: triple quadrupole; UFLC: ultra-fast liquid chromatography; UHPLC: ultra high-performance liquid chromatography; UV: ultraviolet; WWTPs: wastewater treatment plants; π–π EDA: π–π electron donor-acceptor.

Abstract

Saccharin (SAC) is an emerging contaminant, widely detected in the environment, with potential ecotoxicity risks to aqueous organisms and human beings. Wastewater treatment plants (WWTPs) are key sources and sinks of SAC, and play a vital role in eliminating SAC entering the environment. An overview is provided of the potential ecotoxicity of SAC, its occurrence in the aqueous environment, and its degradation performance in WWTPs. SAC treatments, including physical, chemical (mainly advanced oxidation processes AOPs), biological, and hybrid processes, and possible degradation mechanisms are also considered. Of the various SAC removal processes, we find that adsorption-based physical methods exhibit relatively poor performance in terms of SAC removal, whereas chemical methods, especially hydroxy radical-mediated oxidation processes, possess excellent capacities for SAC elimination. Although biological degradation can be efficient at removing SAC, its efficiency depends on oxygen supply and the presence of other co-existing pollutants. Hybrid aerobic biodegradation processes combined with other treatments including AOPs could achieve complete SAC reduction. Furthermore, novel adsorbents, sustainable chemical methods, and bioaugmentation technologies, informed by in-depth studies of degradation mechanisms and the metabolic toxicity of intermediates, are expected further to enhance SAC removal efficiency and enable comprehensive control of SAC potential risks.

Keywords: artificial sweeteners; water treatment; micro-contaminants; absorption; advanced oxidation process; aerobic degradation

1. Background

Artificial sweeteners (ASs) have recently been recognized as emerging micro-contaminants because of their environmental persistence and widespread detection in the aqueous environment (Lange et al., 2012; Scheurer et al., 2010; Weihrauch and Diehl, 2004). ASs are widely consumed in considerable quantities nowadays as sugar substitutes because of their high-intensity sweetness (Kroger et al., 2006; Subedi and Kannan, 2014). Saccharin (SAC) is one of the most popular artificial sweeteners owing to its low price, and sweetness that is about 300 times greater than sugar (**Table 1)** (Lange et al., 2012). Having been approved by several food and drink regulators, including the Food and Drink Federation, SAC is widely consumed by humans as a calorie-free artificial sweetener in more than 90 countries (Kulkarni, 2018). It is believed that SAC may pass unchanged through the human body, and then reach wastewater treatment plants (WWTPs) as domestic effluent, after which the treated effluent provides the main source of SAC in receiving water bodies from which it can be abstracted and recirculated as drinking/tap water (Buerge et al., 2011; Scheurer et al., 2010). Moreover, SAC and its salts (such as saccharin sodium, also called SAC in the literature) are applied in substantial concentrations in nickel-plating, personal care and pharmaceutical products, antiseptics, preservatives, antistatic agents, feeds, *etc*. (Buerge et al., 2011; Cohen et al., 2008; Rashidi and Amadeh, 2009; Spoelstra et al., 2016; Watanabe et al., 2015; Zygler et al., 2009).

[**Table 1**]

SAC has been the focus of a gradually increasing controversy since it was first synthesized in 1879 (Cooper, 1985; Weihrauch and Diehl, 2004). The primary issue associated with SAC was its adverse effects on animals (e.g. carcinogenesis), and therefore probably on humans (Cooper, 1985). Increasingly, environmental and public health concerns have been raised about SAC on account of its long-term application, wide detection in the aqueous environment, and its low, but not negligible, hazard and risk potential to aquatic organisms (Luo et al., 2019). SAC may be a weak carcinogen causing cancer of the urinary tract, even bladder tumors in male rats (Oser, 1985; Uçar and Yilmaz, 2015). SAC-fed zebra fish have experienced elevated levels of cholesteryl ester transfer protein activity in hypercholesterolemia (Kim et al., 2011). SAC may also be one of the main causative factors behind paediatric inflammatory bowel disease, by disturbing gut bacteria (Li et al., 2016; Qin, 2012, 2016, 2019) . Previous studies have also suggested that SAC can induce liver inflammation in mice (Bian et al., 2017). Negative effects of SAC have also been observed on plants, whereby SAC promotes an increase in the micronucleus of plant roots, the higher concentration indicating greater geno-toxicity of certain compounds (Ma et al., 1995) with concomitant cytotoxic and mutagenic impacts on plants (Oliveira et al., 2017). Furthermore, Davididou et al. (2019) found that the degradation products of SAC, having undergone transformations after exposure to solar radiation, were more environmentally toxic than the parent compound SAC, based

on chronic toxicity assessment by monitoring *Vibro fischeri* bioluminescence. SAC is also a major soil metabolite of certain sulfonylurea herbicides, and so could seep into groundwater, eventually contaminating natural waterbodies such as rivers and lakes (Buerge et al., 2011). Therefore, the elimination of SAC from the aquatic environment is of utmost importance.

A comprehensive study focusing on the fate and mitigation strategies of saccharin in water matrix is still a missing element from literature. Such a study could provide a coherent body of knowledge on the topic, guidance for future research, and guidelines for policymakers and stakeholders. With this in mind, the aim of the present work is to review analytical methods for determining SAC, the occurrence and distribution of SAC in aqueous environment, and the efficiency of several SAC elimination approaches.

2. Review methodology

Given that SAC is hydrophilic, we consider the aqueous environment to act as a key sink of SAC. Taking this perspective, "saccharin", "water", and "wastewater" were used as topic words in searching for papers and patents in Web of Science, Scopus, and Google Scholar (as supplementary) without restriction on publication date. Related documents (>100) were selected to summarize research findings on the identification, occurrence, and distribution of SAC in the aqueous environment. We also examined research into applied and potential SAC treatment technologies and their mechanisms for SAC degradation in water and wastewater processes.

3. Results and discussion

3.1 Analytical methods for SAC quantification

A highly-sensitive, accurate method for SAC determination is an important prerequisite for carrying out detailed investigation into the fate of SAC at trace levels from ng/L to μg/L in the aqueous environment. Most recent studies of water and wastewater quality have placed emphasis on physicochemical indicators (such as pH, color, temperature, odor, *etc*.), chemical oxygen demand (COD) content, nitrogen and phosphorus nutrient levels, and concentrations of toxic chemicals (such as heavy metals, persistent organic pollutants (POPs), endocrine disrupting chemicals (EDCs), *etc*.). However, few studies have been reported on the measurement of emerging contaminants with unknown negative effects on environmental and human health (Pal et al., 2014). Given that there is no existing national or international standard method for SAC determination in water samples, a summary of current knowledge on sensitive, accurate methods for SAC determination follows.

To date, analytical techniques for SAC determination in water samples mainly comprise capillary electrophoresis (CE), electroanalysis, flow injection analysis (FIA), gas chromatography (GC), high-performance liquid chromatography (HPLC), reversed-phase HPLC (RP-HPLC), ultra-fast liquid

chromatography (UFLC), ion chromatography (IC), and spectroscopy with thin-layer chromatography (TLC). Different combinations of these analytical techniques have led to more sensitive, accurate methods for determining SAC in water samples or liquids extracted from solid samples. **Table 2** lists the different techniques along with their limits of detection (LODs), and limits of quantitation (LOQs). Determination methods for other ASs or compounds with similar structure to SAC have also been reported and may be considered as alternative SAC determination methods. Examples are LC-ESI-MS/MS (Richter et al., 2007) and ultra HPLC-Q-TOF-MS (UHPLC-Q-TOF-MS) (Russo et al., 2020). Among all the aforementioned techniques, LC-MS/MS has been most widely employed for determining SAC not only in water samples but also in samples prepared by solid phase extraction (SPE) (Arbeláez et al., 2015b; Gan et al., 2013b; Lakade et al., 2018; Ordóñez et al., 2012) or dispersive solid-phase extraction (d-SPE), which are commonly used for extracting target substances from solid phases at concentrations of order mg/L and placing into aqueous samples (Chen et al., 2012; Lakade et al., 2018; Zhao et al., 2013).

[**Table 2**]

For LC-MS/MS, the LODs and LOQs, which indicate instrument sensitivity and accuracy, depend on the performance of the applied liquid chromatography LC and mass spectrometer (MS), the characteristics of the aqueous samples, and operational and environmental factors (**Table 2**). Using SPE-LC-MS/MS, LODs reported for SAC have been in the range of 0.001–0.04 g/L for river water and 0.01–0.5 g/L for influent and effluent wastewater (Arbeláez et al., 2015b). For LC-MS/MS coupled with an electrospray ionization (ESI) source, both the LODs and LOQs were reported to be in the range < 0.015 to 23 ng/L in analyzing wastewater, surface water, and groundwater samples from Vietnam, The Philippines, and Myanmar (Watanabe et al., 2016), and LOD of 0.2 ng/L and LOQ of 0.5 ng/L for surface water and groundwater samples in a separate study (Edwards et al., 2019). For LC-MS/MS using polymeric reversed-phase and mixed-mode with either weak or strong anionic-exchange sorbents, the LOQs for SAC determination obtained for wastewater and surface water samples were in the range 0.01-0.5 g/L (Ordóñez et al., 2012). dSPE-UFLC-MS/MS analysis confirmed the presence of nine food additives in red wine, with the results showing that the LOQs for SAC were 0.10-50.0 g/L (Chen et al., 2012). Using HPLC-MS/MS, sensitive detection of SAC in groundwater and surface water was achieved to about 10 ng/L (Berset and Ochsenbein, 2012). However, the LOD of SAC using HPLC-MS/MS after on-line SPE applied to groundwater samples from a landfill site was 0.0003 g/L (Stefania et al., 2019). Gan et al. (2013b) used IP-LC-TQMS to determine artificial sweeteners including SAC, and found that the method quantitation limits varied between 0.4 and 7.5 ng/L for different water samples. Another analytical method for the determination of six artificial sweeteners in sewage sludge, based on pressurised liquid extraction (PLE) with water, followed by SPE and subsequent LC-MS/MS, indicated that LOQ was 16

ng SAC/g dry weight of sludge (Ordoñez et al., 2013). Kokotou and Thomaidis (2013) used hydrophilic interaction LC-MS/MS to detect and quantify eight artificial sweeteners in wastewater, and reported an instrument LOD of SAC of 0.24 mg/L. Using an isotope-dilution mass spectrometry (IDMS) LC-MS/MS method for quantifying four artificial sweeteners, including SAC, in Finnish surface waters, Perkola and Sainio (2014) recorded LOD of 4.0 ng/L and LOQ of 25.0 ng/L. In an application of LC-MS/MS coupled with hypercrosslinked particles for extraction of SAC using dSPE from environmental samples, the instrument LODs ranged from 0.05–0.5 μg /L, and the lowest points of the calibration curve were taken as the instrument limits of quantification (ILOQs) (Lakade et al., 2018). Other efficient pre-treatment procedures that have been developed, such as direct-injection (DI) HPLC–MS/MS (Berset et al., 2010; Berset and Ochsenbein, 2012; Ochsenbein et al., 2008), are potential candidates as SAC determination techniques.

3.2. Occurrence and distribution of SAC in aqueous environment

To date, research studies have not only focused on method accuracy and sensitivity but also its applicability to the analysis of actual aqueous matrices containing SAC, such as municipal wastewater, waste activated sludge, surface water, groundwater, and potable water.

Table 3 summarizes the overall occurrence and distribution of SAC based on current determination methods.

[**Table 3**]

From the information listed in **Table 3** and given in the open literature, it can be seen that WWTPs are a major source of SAC discharged into environmental waters (Subedi et al., 2014). SAC concentrations in the influent of WWTPs vary according to geographical region; for instance, SAC concentrations have been measured as 9.3-389.0 μg/L in Asia, 1.9-25.1 μg/L in North America, and 7.1-18.0 μg/L in Europe (Tran et al., 2018). WWTPs therefore play a vital role in preventing and controlling the ecological environmental risk induced by SAC. Biological treatment processes, especially the conventional activated sludge process and membrane reactor systems, are still the most commonly applied in existing WWTPs. However, although SAC is readily biodegraded, it is still detected in treated effluent from WWTPs and in sewage sludge (waste activated sludge) (Scheurer et al., 2010; Tran et al., 2014b). Consequently, SAC is consistently detected in surface waters receiving effluent from WWTPs, ground water at locations where sewage sludge has been applied as soil fertilizer, and karst aquifers suffering infiltration by wastewater-polluted surface water (Buerge et al., 2011; Edwards et al., 2019). Therefore, there is an urgent need for better technologies to eliminate SACs from the aquatic ecosystem.

3.3. Treatment technologies for SAC elimination

To reduce the potential adverse effects and ecotoxicity of SAC on aqueous organisms, efficient approaches are imperative in eliminating SAC from water and wastewater. **Table 4** briefly reviews the present state-of-the-art of SAC treatment technologies, and associated degradation mechanisms, classified in terms of the physical, chemical and biological processes involved. A more detailed description follows.

[**Table 4**]

3.3.1 Physical methods

Of the physical treatment methods (**Table 4**), adsorption is the most commonly applied process for SAC removal. Adsorption performance relies primarily on adsorbent type(s) and operational conditions, such as pH, and temperature.

3.3.1.1 Activated carbon (AC)

Activated carbon (AC) is an adsorbent that is effective (due to its non-polar nature) at separating many types of chemicals (especially organics) from the water environment, and has been widely utilized in water and wastewater treatment processes (Bernardo et al., 2006). Applications of AC with or without enhancement to SAC elimination have also been investigated (Bernardo et al., 2006; Li et al., 2018b; Mailler et al., 2015; Scheurer et al., 2010). Bernardo et al. (2016) observed that the SAC removal rate by AC adsorption for 16 h increased from 40% to 75% after enhancement by ultrasonication pretreatment at 500 kHz frequency in argon and O_2/N_2 (20/80 vol%), owing to decomposition of SAC into other compounds that could easily be absorbed by AC when subjected to ultrasound. Li et al. (2018b) achieved a higher removal efficiency of SAC by granular AC (GAC) than for other ASs, such as aspartame (ASP), sucralose (SUC), acesulfame (ACE), cyclamate (CYC), with the removal rate fitting well with SAC's octanol-water partition coefficients-log K_{ow} (**Table 1**). Using a filter with powdered AC (PAC), Mailler et al. (2015) achieved SAC removal rates between 33-54%, and observed that efficient removal performance strongly depended on the PAC filter preload, and the combined effects of adsorption by GAC/PAC and biodegradation by microorganisms on GAC/PAC (Scheurer et al., 2010).

3.3.1.2 Bank filtration

Bank filtration is a natural attenuation process that removes or retains SAC in bank soil, based on soil adsorption capacity and simultaneous biodegradation by indigenous microorganisms in the soil. Scheurer et al. (2010) studied the performance of this process in conventional multi-barrier drinking water treatment plants (DWTPs) for ASs removal and found that SAC was eliminated efficiently (nearly 100%) in all waterworks that employed biologically active bank filtration. However, SAC is hydrophilic, and so

biodegradation might contribute more than soil adsorption to the bank filtration process (Buerge et al., 2011). A study of sand (mainly quartz sand and anthracite) filtration in China has also revealed less efficient SAC removal (14.5%) by adsorption of the main filtration media because of the hydrophilic properties of SAC (Gan et al., 2012).

3.3.1.3 Resins

Resins are cost-efficient absorbing materials with porous structures that perform well in ultrapure water preparation and the advanced treatment of micro-contaminants, POPs, EDCs, and heavy metals (Wang et al., 2010). Recently, resins have also been evaluated for SAC removal; Li et al. (2018b) reported that the amount of SAC adsorbed by an applied magnetic anion-exchange resin was 3.33-18.51 times that of GAC under the same experimental conditions. Li et al. also treated three other ASs (ACE, CYC and SUC), and found that resin adsorption was more efficient at ACE removal, illustrating the importance of resin type in the removal of different kinds of ASs.

3.3.1.4 Reverse Osmosis (RO)

Reverse osmosis (RO) is a membrane separation process aimed at the removal of ions and organic matter, and can produce high quality water for reuse (Dialynas et al., 2008; Li et al., 2020). Nevertheless, when RO was tested for SAC removal in an advanced water recycling plant, the observed removal efficiency was unsatisfactory because of the high water solubility of SAC and the proximity of its molecular weight (183 Da) to that of the cut-off molecular weight of the RO membrane (Busetti et al., 2015). Interestingly, RO achieved an excellent removal rate (>97%) for another sweetener, SUC (Lee et al., 2012). This suggests that RO performance for ASs elimination depends on both the molecular weight and the solubility of the ASs. Furthermore, high energy consumption and membrane fouling rates make RO less cost-effective for large-scale water and wastewater treatment applications.

3.3.1.5 Other physical approaches

Novel absorbents, such as highly porous metal-organic framework (MOF) (Seo et al., 2016) and metal azolate framework-6 derived porous carbons (MDCs) (Song et al., 2018) have been used to remove SAC. MOFs modified by urea and melamine and MDCs have achieved high SAC adsorption performances in water treatment processes, in both cases due to H-bonding on the surface of functional groups. Biochar (BC), an absorbent used in decontamination of water and wastewater (Wang and Wang, 2019), was also tested for SAC removal, and relatively higher sorption of SAC was obtained (Liu et al., 2019). It was shown by Inyang and Dickenson that the π–π stacking interaction between the SAC aromatic ring and the aromatic structure of graphene in BC made a significant contribution to SAC adsorption. Also, the π–π electron donor-acceptor (π–π EDA) interaction occurring between electron-withdrawing sulfonamide and carbonyl functional groups (π electron acceptors) in SAC and the π-electron-rich BC

(π-electron donors) is also believed to play a part in efficient SAC adsorption by BC (Inyang and Dickenson, 2015). Whereas these results were obtained from bench tests, further studies are needed at pilot-scale and, importantly, full-scale operating conditions. Finally, although other new absorbents (*i.e.*, lignite, xylit) and coagulants (*i.e.*, Al^{3+}) for ASs removal have recently been proposed, their adsorption and/or coagulation capacities for SAC removal have proved relatively low or remain unknown (McKie et al., 2016; Rostvall et al., 2018). This suggests that further selection and application of new absorbents for SAC physical removal should be carried out.

3.3.2 Chemical treatments

To date, chemical treatment processes have proved to be the most efficient way to remove organic trace pollutants and thus eliminate their metabolite ecotoxicity. **Table 4** lists the chemical processes used to treat SAC, which are described in more detail below.

3.3.2.1 Chlorination

Chlorination is a widely used disinfection technology applied mainly to inactivate pathogenic microorganisms in DWTPs, water reclamation plants, and WWTPs. (Jia et al., 2015; Li et al., 2017). Studies that introduced chlorination in SAC treatment have found that SAC and other ASs (*i.e.* ACE, CYC, SUC) were persistent and not transformed by the chlorination process, possibly caused by a lack of electron-rich sites for oxidation (Scheurer et al., 2010; Soh et al., 2011; Torres et al., 2011). However, it was found that ACE degradation during chlorination followed pseudo-first-order kinetics and was pH-dependent, and that chlorinated ACE could be the precursor of several regulated disinfection by-products and inhibit *Vibrio fischeri* luminescence (Li et al., 2017). The study also concluded that, although the chlorination process is cost-effective and widely applied, chlorine-related ecotoxic risks should be carefully considered and evaluated. Therefore, more efficient, less eco-risky advanced oxidation processes (AOPs) have been tested for SAC removal; AOPs, including ozonation, UV and Fenton treatment, are based on the *in situ* generation of strong oxidants, mainly hydroxyl-radicals (·OH), for the oxidation of organic compounds (Miklos et al., 2018).

3.3.2.2 Ozonation

Ozonation is one of the most robust advanced oxidation processes (AOPs) for eliminating organic contaminants in wastewater (Xiao et al., 2015). The primary oxidation mechanisms for ozonation are pH-dependent: in acidic conditions, ozone acts as the main oxidant and can react directly with organics, whereas in neutral and alkaline conditions, radicals (mainly ·OH) are formed, initiating oxidation reactions (Pak et al., 2016). Ozone can oxidize a wide range of organics, including those containing aromatic and/or amine-groups (Comninellis et al., 2008; Hollender et al., 2009; Stefan, 2017), and so it has been adopted to remove ASs. A study of multi-barrier DWTPs reported low performance for SAC

removal when reacting directly with ozone instead of its radicals, whereas ozonation was found to degrade ACE well, with moderate removal of SUC, depending on the operating conditions, including ozone concentration and co-existing competing contaminants (Scheurer et al., 2010; Shao et al., 2019). Similar test results indicated that SUC could be degraded significantly through ozonation by radical-mediated oxidation with a relatively high ozone dose (Hu et al., 2017; Lee et al., 2012; Torres et al., 2011). The higher removal efficiencies of ACE and SUC than of SAC might be attributed to the higher oxidation capacity of ·OH (~2.80 V) compared with ozone (~2.07 V).

3.3.2.3 Ultraviolet (UV) irradiation

Ultraviolet (UV) irradiation has been applied to the disinfection and photolysis of organics, exploiting the fact that radiation energy in the ultraviolet (UV) region of the electromagnetic spectrum can alter the chemical bonds of organics (Sastry et al., 2000). Although UV irradiation has recently been tested for SAC removal, it was found invalid because of the low molar extinction coefficient of SAC (Busetti et al., 2015; Li et al., 2018b; Perkola et al., 2016). Even so, photocatalytic oxidation, (*i.e.* UV irradiation combined with other oxidants and/or catalysts) has proved efficient for SAC elimination because additional ·OH ions are generated which in turn oxidize organics in water. Li et al. (2018b) compared ASs oxidation processes involving UV/H_2O_2 and UV/sodium peroxydisulfate (PDS) in five full-scale WWTPs for removal of four ASs, including SAC; the influent SAC concentrations ranged from 430 to 27,340 ng/L, and the degradation efficiency was similar for all ASs. However, it has been reported that UV/PDS performed better than UV/H_2O_2 with the same oxidant dosage because $SO_4^{\cdot-}$ generated from UV/PDS has stronger redox potential (up to 3.10 V at neutral pH, and ·OH of 2.80 V from UV/H_2O_2) and higher selectivity to organic compounds (Xu et al., 2016). Davididou et al. (2017) investigated photocatalytic treatment of SAC under UV irradiation in the presence of TiO_2 nanocomposites tuned by Sn (IV) (which absorbs UV light to produce electrons near the conduction band and holes near the valence band (El-Mekkawi et al., 2020)), and found that photocatalytic performance correlated positively with catalyst loading (up to 400 mg/L) for SAC removal, following a pseudo-first order kinetic rate. Davididou et al. (2018) also assessed the performances of UV-light-emitting diode (LED) and conventional UV-black light (BL) technologies for SAC removal in the presence of TiO_2, exploiting the generation of highly reactive species (mainly ·OH) when photocatalysis is initiated by UV illumination on TiO_2. Data analysis showed that UV-LED was 16 times more energy efficient than UV-BL (Davididou et al., 2018); the enhanced performance of UV-LED was most likely due to the addition of hydroxyl radicals in the aromatic ring, leading to hydroxylated products during photocatalytic transformation (Toth et al., 2012). A contemporaneous study (Zelinski et al., 2018) observed that more than 99% of SAC could be degraded and up to 49% mineralized by TiO_2/UV-A, and, importantly, demonstrated the low toxicity of the photocatalyzed solution of SAC using the *Artemia salina* test. Zelinski et al. also found that UV-

LED in the presence of TiO_2 also achieved very high degradation efficiency (up to 90%) of ACE compared with other photocatalytic processes using UV-LED with ZnO, H_2O_2, peroxomonosulfate (PMS) and PDS, respectively. Furthermore, the ACE degradation rate in UV-LED photolysis process could be enhanced by addition of catalysts and/or oxidants (Wang et al., 2019). Further pilot tests are clearly needed concerning the cost-effectiveness of UV-LED and water ecotoxicity during the oxidation process.

3.3.2.4 Fenton treatment

The Fenton reaction, a widely applied AOP for removal of organics and inorganics from the aqueous environment, was discovered by H.J.H. Fenton in 1894 and consists of reactions of peroxides (mainly H_2O_2) with ferrous ions (Fe^{2+}) to generate active species (usually ·OH) as strong oxidants for the oxidation degradation of pollutants (Fenton, 1894). To date, many attempts have been made to treat wastewater using the Fenton (or Fenton-like) reaction, whereby ferric ions (Fe^{3+}) react with H_2O_2 to produce Fe^{2+}, thus promoting oxidation (Goldstein et al., 1993; Kahoush et al., 2018; Wang, 2008). Recently, the Fenton (or Fenton-like) reaction has been applied to SAC degradation. Chen et al. (2014) utilized photo-Fenton oxidation to degrade saccharin sodium, and reported that TOC decreased by 93% under optimal conditions (500 W mercury lamp, 0.04 g TiO_2, pH = 7, and photo-Fenton ratio of SAC:H_2O_2:Fe^{2+} = 5:60:1). Davididou et al. (2019) investigated SAC removal in a solar compound parabolic collector pilot plant using conventional photo-Fenton at pH 2.8 and olive mill wastewater (OMW)-assisted photo-Fenton. Although higher SAC degradation was achieved by conventional photo-Fenton, encouraging results were obtained using the more sustainable photo-Fenton process with OMW as an iron chelating agent. Moreover, Lin et al. (2016) employed an electro-Fenton process to remove SAC from the aqueous environment, and observed that the SAC degradation rate driven by electrochemically generated ·OH ions followed pseudo-first order kinetics in the presence of Pt and a boron-doped diamond anode. Importantly, the toxicity of treated solution with oxalic, formic, and maleic acid as aliphatic byproducts of SAC was also eliminated after 60-min electro-Fenton reaction (Lin et al., 2016). Excellent ASP degradation performance can be achieved using electro-Fenton reaction, depending on Fe^{2+} concentration and applied current (Richards et al., 2017). Nowadays, growing attention is being paid to sustainable Fenton processes, such as Bio-Fenton, Bio-Electro-Fenton, and Electrochemical/α-FeOOH/PDS approaches; however, further investigations are required in order to better evaluate their SAC degradation efficiencies (Kahoush et al., 2018; Li et al., 2019).

All in all, although AOPs appear attractive as effective technologies for SAC elimination, their performance should be assessed not only in terms of SAC removal, but also in terms of ecotoxicity variation during reaction processes.

3.3.3. Biological degradation and uptake

Biodegradation and uptake, comprising degradation, assimilation, and utilization during biological

metabolisms or activities, are cost-effective, eco-friendly processes that are widely applied for contaminants removal from environmental media (Gaur et al., 2018). Several studies, listed in **Table 4**, have investigated the SAC biodegradable potential of pure strains, mixed microbial communities, and environmental media with rich biodiversity (Richards et al., 2017; Scheurer et al., 2014; Slavič et al., 2018).

3.3.3.1 Bacteria and plants

As reported in 2003, an aerobic bacterium strain, *Sphingomonas xenophaga* SKN, was isolated from domestic sewage and proved to degrade SAC well, with catechol providing the sole source of carbon and energy for growth (Schleheck and Cook, 2003). Later, it was discovered that efficient degradation of SAC involved the participation of both heterotrophic and autotrophic nitrifying microorganisms along with various non-specific oxidative enzymes, and that there was an observable linear relationship between nitrification rate and co-metabolic biodegradation rate (Tran et al., 2014b). *Coliform* bacteria and spoilage bacteria have been identified as being responsible for SAC degradation in drinks (Kabir et al., 2018). Besides, there is a growing body of research suggesting that a substantial proportion of SAC could be degraded by soil microorganisms (Biel-Maeso et al., 2019; Richards et al., 2017; Van Stempvoort et al., 2011a). Recent genomic resolution of bacterial populations in SAC degradation processes has revealed that the dominant saccharin-degrading consortia comprised β-proteobacterial genome from the *Rhodocyclaceae* family (Deng et al., 2019). Larger-scale plants have also proved effective at SAC removal from contaminated soil (Baalbaki et al., 2017). The foregoing indicates an opportunity whereby microorganisms and plants could be isolated and/or enriched in water and applied in wastewater treatment processes to efficient degradation of SAC pollutants.

3.3.3.2 Activated sludge/consortia

The behavior of SAC in water and wastewater treatment processes, especially biological processes encountered in activated sludge systems and membrane bioreactors, has been studied extensively. Buerge et al. (2009) provided evidence for the high aerobic biodegradation of SAC (mean elimination efficiency of 90%, confirmed by Subedi and Kannan (2014) and Tran et al. (2015)) in WWTP activated sludge incubation experiments, with no elimination observed in sterile conditions. Buerge et al. also found that ACE and SUC exhibited persistence with no degradation within 7 h, whereas SAC was degraded by 78% in 3 h under the same operating conditions. Another systematic, bench-scale study (Scheurer et al., 2010) found SAC to be more readily biodegradable in a fixed-bed bioreactor, with complete elimination within 20 d, but hardly any degradation of ACE and SUC even after 92 d. Research on SAC removal in artificial wetlands has also provided evidence that SAC removal is positively correlated ($p < 0.05$) to dissolved oxygen concentration (Vymazal and Dvořáková Březinová, 2016). Complete SAC removal has also been observed in sequencing batch reactors (SBRs), where the presence of SAC had no impact on the removals

of COD, ammonia nitrogen, and total nitrogen (Li et al., 2018a). In a study of primary sludge anaerobic digestion, Phan et al. (2018) observed that SAC was mainly removed in the aqueous phase during anaerobic digestion. In a similar study, Buerge et al. (2011) measured more than 95% SAC removal during the fermentation process, but no SAC removal from the digested sewage sludge. Differences between the microbial communities in the two foregoing studies might be the main reason for the dissimilar SAC removal efficiencies. Future research is needed assessing factors influencing SAC biodegradation performance (e.g. temperature, pH, and hydrodynamics) in treatment units for saccharin sodium and other ASs (Baalbaki et al., 2017; Qu et al., 2019; Shreve and Brennan, 2019).

Overall, biodegradation plays an important part in aqueous SAC treatment, and more advanced molecular biotechnologies could be used to improve efficiency of biological SAC removal. However, given that SAC can accumulate in sludge (Subedi et al., 2014), more attention should be paid to sludge treatment *per se*, which is another important environmental issue worldwide.

3.4. Integrated processes

As described above, treatment approaches based on physical, chemical, and biological principles have particular merits and drawbacks for SAC removal. Hybrid processes, also known as multi-technology processes, are being applied to eliminate SAC ecotoxicity in DWTPs and WWTPs. A popular combination of processes comprises flocculation, sand filtration, AC, or biological treatment (e.g. biosorption, biodegradation), and disinfection by chlorination, ozonation, or UV irradiation in DWTPs (Gan et al., 2012; McKie et al., 2016; Scheurer et al., 2010). Primary (flocculation, sedimentation, *etc.*), secondary (mainly biological degradation under aerobic, anoxic, or anaerobic conditions), and tertiary (disinfection using chlorine, ozone and UV) treatments are the three serial processes that constitute many WWTPs (Buerge et al., 2009; Li et al., 2018b; Subedi and Kannan, 2014; Tran et al., 2015).

For DWTPs, although SAC removal through adsorption is not efficient, the biodegradation of SAC performs well during filtration with active microorganisms located in and on the surface of porous filters (Buerge et al., 2011; Gan et al., 2012; Scheurer et al., 2010). The foregoing studies reported that disinfection by chlorination, ozonation, and UV irradiation exhibited poor/moderate SAC removal, but achieved better degradation performance of ACE.

For WWTPs, more than 90% of SAC could be removed in primary and secondary processes, with biodegradation a key mechanism; however SAC in tertiary treatment would undergo less transformation than other ASs, such as ACE and SUC (Buerge et al., 2009; Li et al., 2018b; Subedi and Kannan, 2014; Tran et al., 2015). This suggests that improving SAC biodegradation efficiency is of great importance in water and wastewater treatment practice.

3.5 Future research

Following this extended literature review on SAC detection, occurrence, and treatment in water,

recommendations for future studies can be drawn, as described below. Given that WWTPs are a major source of SAC discharged into environmental waters (Subedi et al., 2014), emphasis should be placed on developing an efficient technology to eliminate trace amounts of SAC. Advanced oxidation and biological degradation processes seem presently to be a better option than physical processes because of the high hydrophilicity of SACs. During advanced oxidation it is important to evaluate the eco-toxicity of intermediate metabolites from SAC degradation along with its removal efficiency, noting that toxicity is linked with the presence of degradation products (Davididou et al., 2019). Also, further studies are needed to investigate the interaction relationship between SAC and co-existing pollutants, given that SAC co-exists in practice with other pollutants, such as nutrients, ACE, SUC, and other emerging pollutants, some of which exhibit strong reactivity (Scheurer et al., 2010; Shao et al., 2019; Tran et al., 2014b). Inspired by the synchronous biodegradation of various pollutants in soil and activated sludge, biological processes offer a great opportunity in practice as cost-effective SAC removal methods; further research is recommended to isolate certain functional strains to enrich dominant biological communities that are key to water and wastewater treatment processes (Baalbaki et al., 2017; Biel-Maeso et al., 2019).

4. Conclusion

This state-of-the-art review has examined the current understanding of SAC degradation processes and the occurrence and distribution of SAC, determined primarily by LC-MS/MS and other novel or modified technologies. As an emerging contaminant, SAC appears not as safe as believed previously, owing to its worldwide long-term, large volume consumption, its ubiquitous detection in environmental media, and its potential chronic eco-toxicity. It was observed that although there is no existing national or international standard method for SAC determination in water samples, accurate methods for SAC determination have been recently developed. Based on these analytical techniques, several studies confirmed the occurrence of SAC at WWTP discharges worldwide at the μg/L order, indicating that treatment plants play a vital role in preventing and controlling the ecological environmental risk induced by SAC. Extensive research on physical, chemical, and biological technologies for SAC has been carried out. Among these techniques, advanced oxidation and biological processes appear to be efficient ways to eliminate SAC in water matrix. Regarding future research, the focus should be placed on the ecotoxicity of SAC degradation products as well as its interaction with other co-existing water pollutants. Moreover, the isolation and application of functional strains to enrich dominant biological communities may be key to development of successful biological processes for wastewater treatment. In all cases, a cost-benefit analysis of SAC treatment would be recommended before scaling up the process.

Declaration of competing interest

The authors declare no conflict of interest.

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Table

Table 1 Physicochemical properties of saccharin

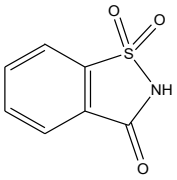
Name	Structure	Properties	Acceptable daily intake
Saccharin (1,1-dioxo-1,2-benzothiazol-3-one; Benzoic sulfimide)		CAS No.: 81-07-2; Chemical formula: $C_7H_5NO_3S$; Molecular weight: 183.18 g/mol; pK_a : 2.2; log K_{ow} : 0.91; Water solubility: 4 g/L	5 mg/kg body weight (sodium salt); 3.8 mg/kg body weight (free acid)

Table 2. Analytical techniques with limits of detection (LODs) and limits of quantitation (LOQs) for SAC detection in different aqueous samples.

Analytical technique	**Water matrix**[a]	**LODs** (μg/L)	**LOQs** (μg/L)	**Reference**
High-pressure LC	Animal feed	N/A[b] (low to 10 ppm)	N/A	(Holder and Bowman, 1980)
	Human urine	N/A (low to 10 ppm)	N/A	
	Wastewater	N/A (low to 0.1 ppm)	N/A	
LC-tandem mass spectrometry (MS/MS) (LC-MS/MS)	Surface water	N/A	0.25	(Ordóñez et al., 2012)
	Wastewater	N/A	0.50	
	Tap water/Wastewater	0.24 (instrument)	0.80 (instrument)	(Kokotou and Thomaidis, 2013)
	River water	0.001-0.04	N/A	(Arbeláez et al., 2015b)
	Wastewater	0.01-0.5	N/A	
	Groundwater	0.3	N/A	(Stefania et al., 2019)
LC with electrospray ionization source equipped MS (LC-ESI-MS)	River/Wastewater	1.5×10^{-5}-0.023 (instrument)	1.5×10^{-5}-0.023 (instrument)	(Watanabe et al., 2016)
LC time-of-flight MS (LC-TOF-MS)	Soft drink and liquid (no extraction)	100 (instrument)	1000 (instrument)	(Ferrer and Thurman, 2010)
	Ground/surface/waste water	0.5 (instrument)	5 (instrument)	
LC-quadrupole(Q)-TOF-MS	Surface/waste water	N/A	N/A	(Hernández et al., 2015)
	Artificial wastewater (filtration)	N/A	N/A	(Davididou et al., 2019)
HPLC-MS/MS	Ground/river/tap/waste water	N/A	0.01	(Berset and Ochsenbein, 2012)
UFLC-Q-MS/MS	Red wine	1.5	5	(Chen et al., 2012)
Ion-pair HPLC triple quadrupole-MS (IP-HPLC-TQ-MS)	River water	0.0003	0.0008	(Gan et al., 2013b)
	Tap water	0.0003	0.0011	
	Sea water	0.0005	0.0018	
LC-isotope-dilution MS (LC-IDMS)	Surface water	0.004	0.025	(Perkola and Sainio, 2014)
LC-high resolution MS (LC-HR-MS)	Artificial wastewater (filtration)	0.005	0.1	(Davididou et al., 2018)
RP-HPLC-Q-TOF-MS	Wastewater	N/A	N/A	(Kempińska and Kot-Wasik,

Analytical technique	**Water matrix**[a]	**LODs** (μg/L)	**LOQs** (μg/L)	**Reference**
				2018)
FIA coupled a monolithic column	Artificial wastewater	N/A	N/A	(Fatibello-Filho et al., 1994)
	Artificial wastewater	1.5×10^{-5} mol/L	N/A	(Fatibello-Filho and Aniceto, 1999)
	Liquid sweetener products	N/A	2.4×10^{6}	(Mendes et al., 2010)
CE with capacitively coupled contactless conductivity detection (C^4D)	Soft drink (filtration)	N/A	10	(Frazier et al., 2000)
	Soft drink (dilution)	1500	4900	(Bergamo et al., 2011)
IC with suppressed conductivity detector	Carbonated cola drink (ultrasonic+dilution)	45	N/A	(Zhu et al., 2005)
	Fruit juice drink (dilution)			
	Preserved fruit (ultrasonic+dilution)			
TLC	Toddy	0.1μg/spot (9 μg/cm^2)	N/A	(Mali et al., 2005)

a. samples in this column all are extracted except those indicated otherwise; **b**. N/A: not applicable.

Table 3 Research information on saccharin occurrence in the aqueous environment including wastewater and sludge in WWTPs and wetlands, surface water, groundwater, runoff, tap water (drinking water), and sea water.

Water Matrix	Location	Year	Range/Concentration (ng/L)	Determination Method	Reference
Wastewater	Karlsruhe, German (WWTPs)	N/A[a]	34,000-50,000 (in[b]); 400 (out[c])	HPLC-ESI-TQ-MS	(Scheurer et al., 2009)
	Zurich, Switzerland (WWTPs)	Jun, Oct 2008	3900-18,000 (in); <LOD-3200 (out)	LC-MS/MS	(Buerge et al., 2009)
	US (WWTPs)	N/A	<LOD-5000 (out)	LC-TOF-MS	(Ferrer and Thurman, 2010)
	Zurich, Switzerland (WWTPs)	N/A	4000-18,000 (in); <100-3000 (out)	LC-MS/MS	(Buerge et al., 2011)
	Switzerland (WWTPs)	May 9-10, 2011	86-16,201 (out)	HPLC-MS/MS	(Berset and Ochsenbein, 2012)
	NW Spain (WWTPs)	Sep 2011	18,400-22,300 (in); 7100-9100 (out)	LC-ESI-TQ-MS	(Ordóñez et al., 2012)
	Athens, Greece (WWTPs)	N/A	15,000-46,000 (in); <LOD-270 (out)	LC-ESI-MS/MS	(Kokotou and Thomaidis, 2013)
	Tianjin, China (WWTPs)	N/A	~10,300 (in); ~242 (out)	IPLC-ESI-TQ-MS/MS	(Gan et al., 2013b)
	Tianjin, China (WWTPs+Wetlands)	Jun 28, 2011; Nov 6, 2011	WWTPs: 7200-9100 (in); 270-280 (out) Wetlands: 140-560	LC-TQ-MS/MS	(Gan et al., 2013a)
	Singapore (WWTPs)	N/A	10^1 -10^6 (in)	HPLC-ID-MS/MS	(Tran et al., 2014a)

Water Matrix	Location	Year	Range/Concentration (ng/L)	Determination Method	Reference
Wastewater	Tianjin, China (WWTPs)	Dec 13-26, 2012; Sep 11-24, 2013	210 ±160 (AVG ±SD)[d]	LC-MS/MS	(Gan et al., 2014)
	Albany, USA (WWTPs)	Jul 12-18, 2013	1860-25,100 (in); 130-15,200 (out)	HPLC-MS/MS	(Subedi and Kannan, 2014)
	Tarragona, Spain (WWTPs)	N/A	<LOQ-155,000 (in); <LOQ-500 (out)	HPLC-ESI-MS/MS	(Arbeláez et al., 2015b)
	India (WWTPs)	Jul-Aug 2012	303,000 (in, highest M[e]); 12,120 (out, removal rate 96%)	HPLC-ESI-MS/MS	(Subedi et al., 2015)
	Singapore (Water reclamation plant)	Feb-Jul 2013	9310-18,797 (in); <LOD (out)	HPLC-MS/MS	(Tran et al., 2015)
	Hanoi, Vietnam (WWTPs)	Oct, Dec 2013	7600-13,000 (in); 23-36 (out)	LC-ESI-MS	(Watanabe et al., 2016)
	Czech Republic (Constructed wetland)	Oct 2013-Nov 2015	6,200-87,000 (in); 2600-37,000 (out, AVG removal rate 42.4%)	UHPLC-ESI-TQ-MS/MS	(Vymazal and Dvořáková Březinová, 2016)
	South German (WWTPs)	2012-2014	14,000 (in, highest M)	HPLC-ESI-MS/MS	(Seitz and Winzenbacher, 2017)
	Ontario (Septic tanks)	N/A	6100-72,000 (single dwelling); 2200-63,000 (multiple dwelling)	IC-ESI-MS/MS	(Snider et al., 2017)
	Pearl River Delta region, South China (WWTPs)	May-Oct 2015	8230 (in, M); <823 (out, removal rate > 90%)	UHPLC-ESI-MS-MS	(Yang et al., 2017)
	Tianjin, China (Farm WWTPs)	Aug 2015-May 2016	781,000 ±9000 (in); 11,100 ±100 (primary out); 5640 ±370 (out)	LC-TQ-MS/MS	(Baalbaki et al., 2017)

Water Matrix	Location	Year	Range/Concentration (ng/L)	Determination Method	Reference
Wastewater	Nanjing/Wuxi, China (WWTPs)	Oct 15, 2015; Jan 15, Apr 15, Jul 15, 2016	430-27,340 (in); 20-240 (out)	UPLC-ESI-TQ-S MS/MS	(Li et al., 2018b)
	Tarragona & Reus, Spain (WWTPs)	N/A	4700-17,900 (out)	HPLC-MS/MS	(Lakade et al., 2018)
	N/A (WWTPs)	N/A	4408-52,962 (in); <LOQ-5663 (out)	HPLC-MS/MS	(Tran et al., 2019)
Sludge	Zurich, Switzerland (Farm WWTPs)	N/A	liquid manure: 3×10^5-1.2×10^7; manure fermentation: 300-5×10^5; sludge:1×10^4-1.6×10^4	LC-MS/MS	(Buerge et al., 2011)
	NW Spain (WWTPs)	N/A	141-255 ng/g dwS[f] (primary); <LOD-124 ng/g dwS (secondary)	LC-ESI-MS/MS	(Ordoñez et al., 2013)
	South Korea (WWTPs, Mixed: Industrial + Domestic)	Jul-Oct 2011	11.4-55.4 ng/g dwS (Industrial); 7.08-3240 ng/g dwS (Domestic); 11.6-54.0 ng/g dwS (Mixed);	HPLC-ESI-TQ-MS/MS	(Subedi et al., 2014)
	Albany, USA (WWTPs)	Jul 12-18, 2013	<LOD-388,000	HPLC-MS/MS	(Subedi and Kannan, 2014)
	Catalonia, Spain (WWTPs)	consecutive 3 months	105-591 ng/g dwS	HPLC-ESI-TQ-MS/MS	(Arbeláez et al., 2015a)
	India (WWTPs)	Jul-Aug 2012	18,700 ng/g dwS	HPLC-ESI-MS/MS	(Subedi et al., 2015)
Surface water	Swiss Midland region	Feb-Mar 2008	<LOD-2800	LC-MS/MS	(Buerge et al., 2009)
	Swizerland	May3,16-19, 2011	<LOQ-310	HPLC-MS/MS	(Berset and Ochsenbein, 2012)
	NW Spain	Sep 2011	<LOD-19,700	LC-ESI-TQ-MS	(Ordóñez et al., 2012)
	Tianjin, China	N/A	193-746	IPLC-ESI-TQ-MS/MS	(Gan et al., 2013b)
	Tianjin, China	Jul 9-15, 2011,	210-1100	LC-TQ-MS/MS	(Gan et al., 2013a)

Water Matrix	Location	Year	Range/Concentration (ng/L)	Determination Method	Reference
Surface water	Ontario, Canada	Jun 14, Sep 5, 2007; Apr 24, 2009	<LOD-7200	IC-ESI-MS/MS	(Spoelstra et al., 2013)
	Singapore	N/A	<LOD-3210	HPLC-ID-MS/MS	(Tran et al., 2014a)
	Finland	Jun, Oct 2011; May, Jun 2012	<25-490	UPLC-ESI-ID-MS/MS	(Perkola and Sainio, 2014)
	Hong Kong, China	Jul 22, 2011; Jan 17, 2012	250	UHPLC-ESI-TQ-MS/MS	(Sang et al., 2014)
	Tianjin, China	Dec 13-26, 2012; Sep 11-24, 2013	120-62,700	LC-MS/MS	(Gan et al., 2014)
	Chennai, India	Jul - Aug 2012	419,000	HPLC-ESI-MS/MS	(Subedi et al., 2015)
	Hanoi/Haiphong Vietnam	Oct, Dec 2013	0.092-17,000	LC-ESI-MS	(Watanabe et al., 2016)
	Manila, The Philippines	Jun 2014	290-9600	LC-ESI-MS	(Watanabe et al., 2016)
	Pathein/Yangon, Myanmar	Dec 2014	<LOD-71	LC-ESI-MS	(Watanabe et al., 2016)
	Barbados, West Indies	Feb, Jun 2013	<LOQ-488±46	LC-ESI-MS/MS	(Edwards et al., 2017)
	River Ebro	N/A	100-200	HPLC-MS/MS	(Lakade et al., 2018)
	Northern Italy	Mar 2017	<LOQ-530	HPLC-MS/MS	(Stefania et al., 2019)
	N/A	Apr 2015-Dec 2016	<LOQ-5663	HPLC-MS/MS	(Tran et al., 2019)
Groundwater	Mediterranean country, German	N/A	<LOD-<400	HPLC-ESI-TQ-MS	(Scheurer et al., 2009)
	Zurich, Swizerland	Aug, Nov 2008	<LOD	LC-MS/MS	(Buerge et al., 2009)
	Canada (Lagoon)	N/A	<LOD-10,300	IC-ESI-TQ-MS/MS (isotope-labled)	(Van Stempvoort et al., 2011b)
	Ontario, Canada	Sep 2008; Jun, Oct 2009; Mar-Apr 2010	21-40,000	IC-ESI-TQ-MS/MS	(Van Stempvoort et al., 2011a)

Water Matrix	Location	Year	Range/Concentration (ng/L)	Determination Method	Reference
	Switzerland	May 23 -24 2011	<LOQ-15	HPLC-MS/MS	(Berset and Ochsenbein, 2012)
	Tianjin, China	N/A	11.3-80.0	IPLC-ESI-TQ-MS/MS	(Gan et al., 2013b)
Groundwater	Barrie/Jasper, Canada	Sep-Nov 2010	<LOD-35	LC-MS/MS	(Van Stempvoort et al., 2013)
	Tianjin, China	Jul 2011	52-63	LC-TQ-MS/MS	(Gan et al., 2013a)
	Singapore	N/A	<LOD-780	HPLC-ID-MS/MS	(Tran et al., 2014a)
	Canada (Landfill monitoring well)	N/A	<LOQ-250,000	IC-ESI-TQ-MS/MS	(Roy et al., 2014)
	Halong, Vietnam	Oct, Dec 2013	<LOD-13	LC-ESI-MS	(Watanabe et al., 2016)
	Barbados, West Indies	Feb, Jun 2013	2.7±0.2 - 9.6±2.1	LC-ESI-MS/MS	(Edwards et al., 2019)
	Northern Italy	Mar 2017	<LOQ -680	HPLC-MS/MS	(Stefania et al., 2019)
Runoff	Gryteland stream, Norway	Nov 2014; Feb, Jun, Sep, Dec 2015; Mar 2016	<LOQ-80 (in); <LOQ-74 (out)	UHPLC-TQ-MS/MS	(Paruch et al., 2017)
	N/A	Apr 2015-Dec 2016	45-9125 (urban) 17-1028 (Agricultural)	HPLC-MS/MS	(Tran et al., 2019)
Tap water	Tianjin, China	N/A	47.5-65.1	IPLC-ESI-TQ-MS/MS	(Gan et al., 2013b)
	Tianjin, China	Jul 2011	Up to 110	LC-TQ-MS/MS	(Gan et al., 2013a)
	Canada	N/A	<LOD-350	IC-ESI-MS/MS	(Spoelstra et al., 2013)
Sea water	Tianjin, China	N/A	99.7-249	IPLC-ESI-TQ-MS/MS	(Gan et al., 2013b)
	Hong Kong, China	Jul 22, 2011; Jan 17, 2012	<LOD-300	UHPLC-ESI-TQ-MS/MS	(Sang et al., 2014)
	Western basin, the Mediterranean Sea	Autumn 2014	0.49-5.23	UPLC-MS/MS; HPLC-MS/MS	(Brumovský et al., 2017)

a. N/A: not applicable; **b**. in: inflow/influent/inlet/raw/untreated water in related references; **c**. out: outflow/effluent/outlet/treated water in related references; **d**. AVG±SD: average concentration ± standard deviation; **e**: M: median concentration; **f**. ng/g dwS: ng/g dry weight sludge.

Table 4. Physical, chemical, and biological processes/techniques for SAC treatment

Treatment technique		Main mechanism	SAC optimal removal performance	Reference
Physical	**Activated carbon (AC)**	Adsorption	**1. AC** (lab-scale) 40% (only AC adsorption 16 h); 75% (ultrasonication 180 min + AC adsorption, 16 h)	(Bernardo et al., 2006)
		Adsorption + Biodegradation (main)	**2. Granular AC (GAC)** (lab-scale) 0.4 mg SAC/g GAC	(Li et al., 2018b)
		Adsorption	**3. Powdered AC (PAC)** (pilot-scale) 33-54% (fluidized bed)	(Mailler et al., 2015)
	Biochar (BC)	Adsorption (π–π stacking)	Partial removal (lab-scale)	(Liu et al., 2019)
	Filtration	Adsorption + Biodegradation (main)	**1. Bank filtration** (sampling study) Nearly 100% (by soil)	(Buerge et al., 2011)
			2. Sand filtration (sampling study) 14.5% (by mainly quartz sand and anthracites)	(Gan et al., 2012)
	Metal-organic framework (MOF)	Adsorption (H-bonding)	**1. Maximum adsorption capacity of MIL** (name for a specially prepared MOF) (lab-scale) 53.4 mg SAC / g MIL-101 70.1 mg SAC / g melamine-MIL-101 86.4 mg SAC / g urea-MIL-101 18.7 mg SAC / g O_2N-MIL-101	(Seo et al., 2016)
			2. Maximum adsorption capacity of metal azolate framework-6 derived porous carbons (MDCs) (lab-scale) 93.3 mg SAC/ g MDC-4h; 99.2 mg SAC/ g MDC-6 h; 94.5 mg SAC/ g MDC-12 h	(Song et al., 2018)

Treatment technique		Main mechanism	SAC optimal removal performance	Reference
Physical	**Resins**	Adsorption	8.1% (magnetic anion exchange resin) (lab-scale)	(Li et al., 2018b)
	Reverse Osmosis (RO)	Adsorption and/or rejection by RO membrane	Very poor (full-scale)	(Busetti et al., 2015)
Chemical	**Chlorination**	Chlorine-based selective oxidation	Poor removal efficiency (field study + lab-scale)	(Scheurer et al., 2010)
	Ozonation	Ozone acts as main oxidant and reacts directly with organics in acidic pH; ·OH, generated from O_3-based reactions, acts as main oxidant with organics in neutral and alkaline conditions	Poor performance (field study + lab-scale), with no obvious SAC removal with O_3 at 0.5 mg/L, 20% of SAC removed only with O_3 at 5 mg/L	(Scheurer et al., 2010)
	Ultraviolet (UV)	Photodegradation induced by radiation energy from UV lights acting on chemical bonds	**1.** N/A (full-scale)	(Busetti et al., 2015)
			2. Poorly photodegraded (lab-scale)	(Perkola et al., 2016)
			3. N/A (lab-scale)	(Li et al., 2018b)
	UV-induced advanced oxidation processes (AOPs)	Oxidation processes between organics and radical (mainly ·OH) induced by reactions among UV, oxidants and/or catalysts	**1. UV/H_2O_2** (sampling study) 3.59×10^{-4}/s (degradation rate constant k_1, degradation followed pseudo-first-order kinetics)	(Li et al., 2018b)
			2. UV/ Sodium peroxydisulfate (PDS) (sampling study) 7.23×10^{-4}/s (degradation rate constant k_1, degradation followed pseudo-first-order kinetics)	
			3. UV/ photocatalysts tuned by Sn (IV) (lab-scale) 98% with catalyst Aeroxide TiO_2 P25; 67% with catalyst CristalACTiV PC105; 43% with catalyst KRONOClean 7050; 21-27% with catalysts pure anatase, 15% rutile and 30% rutile respectively	(Davididou et al., 2017)

Treatment technique	Main mechanism	SAC optimal removal performance	Reference
Chemical		**4. UV/TiO_2** (lab-scale) UV-light-emitting diode (LED)/TiO_2 has higher SAC removal efficiency and is 16 times more energy efficient than UV-blacklight (BL)/TiO_2	(Davididou et al., 2018)
		5. UV-A/TiO_2 (lab-scale) >90 % degraded and 49% mineralized	(Zelinski et al., 2018)
Fenton Treatment	Organics oxidized and degraded by strong oxidants (usually ·OH) generated by reaction of peroxides (mainly H_2O_2) with ferrous ions (Fe^{2+})	**1. Photo/TiO_2-Fenton** (lab-scale) 93 % of TOC removal	(Chen et al., 2014)
		2. Photo-Fenton (lab-scale) 0.05-0.1 L/kJ (reaction rate constant *k*, conventional) 2.21-7.88 L/kJ (reaction rate constant *k*, assisted by Ethylenediamine-N, N-disuccinic acid) 0.13 L/kJ (reaction rate constant *k*, assisted by olive mill wastewater)	(Davididou et al., 2019)
		3. Electro-Fenton (lab-scale) Apparent rate constant k_{app} for SAC degradation: 0.18/min (with dimensionally stable anodes (DSA)); 0.19/min (with platinum (Pt) anode); 0.21/min (with boron-doped diamond (BDD) anode) Mineralization for SAC: 55.8 % (with DSA anode); 76.1 % (with Pt anode); 96.2 % (with BDD anode)	(Lin et al., 2016)

Treatment technique		Main mechanism	SAC optimal removal performance	Reference
Biological	**Bacteria**	SAC as sole carbon and energy sources for bacterial aerobic growth	**1. Pure strain** (lab-scale) Specific growth rate (μ) of 0.14/h of bacterium *Sphinogomonas xenophage* SKN under aerobic conditions, and the substrate utilization concomitant with growth.	(Schleheck and Cook, 2003)
		SAC as source for bacterial growth	**2. Mixed bacteria** (sampling study +lab-scale) Sobo drink containing 0.25g SAC with 50% degradation rate on 12th day; 0.5g SAC with 64.5% degradation rate on 3rd day; 1.0g SAC with 19.3% degradation rate on 12th day; 1.5g SAC with 8.1% degradation rate on 12th day; 2.0g SAC with 3.1% degradation rate on 12th day Bacteria accounting for SAC degradation are common spoilage bacteria and coliform bacteria including *Bacillus subtilis, Bacillus pumilis, Bacillus azotomonas, Micrococcus varians, Aeromonas hydrophila, Enterobacter aeromonas, Lactobacillus acidophilus*.	(Kabir et al., 2018)
		SAC degraded by nitrifying bacteria together with their induced non-specific oxidative enzymes	**3. Nitrifying consortia** (lab-scale) 60-80% SAC degraded by nitrifying community	(Tran et al., 2014b)
		SAC as sole carbon source with microbial enzymes initiating SAC degradation	**4. Consortia from activated sludge in WWTPs** (lab-scale) Complete removal followed zero-order kinetics by consortia dominated by a β-proteobacterial genome from the family *Rhodocyclaceae*.	(Deng et al., 2019)

Treatment technique		Main mechanism	SAC optimal removal performance	Reference
Biological	**Plant**	High water solubility and hydrophilic nature of SAC	Uptake by plants (vegetables, i.e. radish, celery, young celery, spinach and cabbage mustard) significant when SAC occurred at high levels in the surrounding environment (sampling study)	(Baalbaki et al., 2017)
	Activated sludge	SAC as carbon and energy sources of microorganism with different functions and metabolic ways under aerobic conditions. SAC removal performance depends on diversity of microbial community.	**1. Aerobic activated sludge in WWTPs** (full-scale and/or lab-scale) 90% - nearly 100% of SAC degraded under aerobic conditions in bioreactor	(Buerge et al., 2009) (Scheurer et al., 2010) (Subedi and Kannan, 2014) (Tran et al., 2015) (Li et al., 2018a)
			2. Anaerobic sludge in WWTPs *a*. >95% of SAC removal in the fermentation processes but no SAC removal in digested sludge (sampling study) *b*. No SAC degradation under anaerobic digestion (pilot-scale)	(Buerge et al., 2011) (Phan et al., 2018)
			3. Sludge in constructed wetlands (sampling study) 27.1-53.3% by aerobic consortia in constructed wetlands	(Vymazal and Dvořáková Březinová, 2016)